UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,354	04/07/2006	Petra Schulz	37998-237530	2520

26694 7590 06/22/2009

VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
06/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,354	SCHULZ ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received March 10, 2009.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 12-20 are canceled. Claims 1-11 are currently under examination.

Priority: The request for priority to provisional application 60/494097, filed August 12, 2003, is acknowledged.

Objections and Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al. (US 6284874; previously cited). For examination purposes, claim 1 has been interpreted as a process for purifying A1AT from other protein components in an A1AT containing solution comprising: a) subjecting an A1AT containing solution to ion-exchange chromatography; b) then adding detergents; c) increasing the salt concentration to salt out detergents.

Taniguchi et al. teach a method of purifying alpha-1 proteinase inhibitor, also known as α_1-antitrypsin (A1AT), by flow-through chromatography, viral inactivation, and filtration (col. 2-4). In Example 1, Taniguchi et al. teach a plasma fraction of

IV_1+IV_4 was solubilized in PEG/$ZnCl_2$, applied to a QAE anionic-exchange chromatographic column (col. 6 lines 60-65; claim 1a), eluted, and diafiltered (col. 7 lines 1-10). Taniguchi et al. further teach that 1.1 kg of a detergent solution of 10% w/v polysorbital 80 and 3% w/v tri-n-butyl phosphate (TnBP) was added to the diafiltered A1AT and incubated at 25°C for 1 hr. to inactivate any viral contaminants (col. 7 lines 10-15; claim 1b). The A1AT solution was then applied to a copper chelating medium and washed with 150 mM NaCl, 500 mM NaCl (col. 7 lines 20-25; claim 1c). The A1AT solution was the ultrafiltered, filtrate was collected, and diafiltered by ultrafiltration against 50 mM NaCl (col. 7 lines 30-35; claim 5, 9). Taniguchi et al. teach the filter used has a 100 kD MWCO, which is in the range of a filter having a pore size between 15-20 nm (col. 5 line 31-32; claim 10).

In their remarks, Applicants assert (1) the claimed invention is more simple than the method of Taniguchi et al. and does not require PEG/$ZnCl_2$ precipitation, work up of the precipitate and resolubilization. Neither a metal chelate chromatography is used nor mentioned according to the invention. However, this seems to be an essential step for the method of Taniguchi et al. (2) The Examiner seems to interpret "salting out" as any increase in salt concentration of any salt. However, this is not the case. Salting out is known to require a phase separation and depends on concentration and type of salt. Sodium citrate as used in the present application will require a different concentration for a phase separation than sodium chloride, which is used by Taniguchi et al. for washing adsorbed A1AT. (3) An additional indication for the difference between Taniguchi's washing and the salting out of the present application is the fact that A1AT binds to the

metal chelate medium of Taniguchi et al. This interaction definitely interferes with the conditions in solution resulting in facilitation of washing and prohibition of formation of a two or multi-phase system. In other words, to generate an additional phase (i.e. salting out) while A1AT is bound to the chelate medium, it is necessary to apply salt in higher concentrations compared to starting solution. Applicant's arguments have been fully considered but they are not persuasive.

(1a) As noted above, claim 1 has been interpreted to comprise three active steps: a) subjecting an A1AT containing solution to ion-exchange chromatography; b) then adding detergents; and c) increasing the salt concentration to salt out detergents. It should also be noted that steps 1(b) and 1(c) do not specify to what the detergent should be added to, i.e. the ion-exchange column, an A1AT solution, etc. Further, the use of open language "comprising" allows for the inclusion of other unspecified steps and/or ingredients in the claim interpretation. Therefore, while Taniguchi et al. may teach the additional steps as noted in Applicants' remarks, Taniguchi et al. still teach claim steps 1(a), 1(b), and 1(c), as noted above, which includes adding NaCl (increasing the salt concentration) to the A1AT solution after ion-exchange chromatography and addition of TnBP (claim 1(c)). Even if Taniguchi et al. do not explicitly state that adding NaCl will salt out the detergents, the "salting out" process would inherently occur since the salt concentration of the A1AT solution was increased by adding NaCl solution.

(2a) The phase separation of "salting out" with citrate is not recited in claim 1; therefore, an increase in concentration of any type of salt would believe to "salt out" detergent. Since Taniguchi et al. teach adding NaCl (increasing the salt concentration) to

the A1AT solution after ion-exchange chromatography and addition of TnBP, the detergents would inherently be removed.

(3a) See the reasons regarding the use of open language "comprising" in (1a).

For at least these reasons, the Taniguchi et al. reference is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi et al. (US 6284874) in view of Isaksson et al. (WO 9426287; IDS). The teachings of Taniguchi et al. are outlined above. Taniguchi et al. do not teach a heparin gel or a pasteurization step.

Isaksson et al. teach a process for reduction of virus inactivating chemicals and/or detergents in an aqueous composition containing a water-soluble plasma protein (abstract). Isaksson et al. further teach that when the aqueous base comprises a salt of citrate at >1 M, the virus inactivating chemical or detergent can give a final concentration below 5 ppm (abstract). Isaksson et al. teach the method is applicable to any plasma protein (p. 6 lines 15-20). In example I, Isaksson et al. teach the plasma protein antithrombin III (AT III) was separated from plasma by using a heparin sepharose gel (p. 7 lines 15-18). Isaksson et al. further teach an additional virus inactivation step of incubating the plasma protein solution in 2 M sodium citrate (p. 7 lines 20-30).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Taniguchi et al. by substituting the heparin sepharose gel of Isaksson et al. for the anionic-exchange column used in Taniguchi et al. (claims 6-7). One of ordinary skill would recognize that the chromatographic step can be substituted with a functionally equivalent column that is commercially available and would expect to have a reasonable level of success in using a heparin sepharose gel to isolate A1AT because Isaksson et al. disclose its use is successful in separating another plasma protein.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Taniguchi et al. by including the additional virus inactivation step of Isaksson et al. to the A1AT purification process of Taniguchi et al. (claim 8). The motivation to do so is given by Isaksson et al. which disclose that sodium citrate helps in reducing the residual detergent content and therefore, would result in a purer protein product.

In their remarks, Applicants assert (1) the Taniguchi et al. reference does not disclose "salting out" of the detergents according to the claims. (2) The claimed invention is directed to A1AT which is not mentioned in Isaksson et al. It is doubtful that a person of ordinary skill would perform substituting the anionic-exchange column of Taniguchi et al. for the heparin sepharose gel of Isaksson's antithrombin production because one of ordinary skill would not incorporate a purification step used for the production of a different product. A person of ordinary skill would know that steps known for the production of one protein can usually not be applied to the production of

another protein so easily as the Examiner suggests. Applicant's arguments have been fully considered but they are not persuasive.

(1a) The reasons for maintaining the Taniguchi et al. reference is the same as noted above.

(2a) Isaksson et al. disclose that their method is applicable to any plasma protein and discloses some examples of plasma proteins. It is known in the art that A1AT is a plasma protein. Isaksson et al. then disclose a working example using heparin sepharose gel to separate out a specific plasma protein, i.e. antithrombin. Since Taniguchi et al. already teach the successful separation of A1AT by anion-exchange gel, it would be reasonable for one of ordinary skill to substitute various types of anion-exchange gels in order to determine which anion-exchange gel will be the optimum material to use for purifying A1AT. Since Isaksson et al. disclose that the method using an anion-exchange gel can be applied to any plasma protein, one of ordinary skill would be motivated to substitute heparin sepharose for obtaining A1AT (a plasma protein) since Isaksson et al. disclose its successful use in obtaining a different plasma protein.

For at least these reasons, the 103(a) rejection is maintained.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/
Primary Examiner, Art Unit 1656

June 18, 2009